UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE: JOHNSON & JOHNSON TALCUM POWDER PRODUCTS MARKETING, SALES PRACTICES AND PRODUCTS LIABILITY LITIGATION	MDL Docket No. 2738
This Document Relates To All Cases	

DEFENDANTS JOHNSON & JOHNSON AND JOHNSON & JOHNSON CONSUMER INC.'S REPLY IN SUPPORT OF MOTION TO EXCLUDE PLAINTIFFS' EXPERTS' OPINIONS RELATED TO BIOLOGICAL PLAUSIBILITY

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A variety of plaintiffs' experts seek to offer opinions that there is a biologically plausible mechanism by which cosmetic talcum powder applied ***externally*** to the perineum of a woman's body can travel upward through the genital tract, reach her ovaries (or fallopian tubes) and trigger chronic inflammation that then instigates ovarian cancer. But, as explained in defendants' opening brief, each link in the chain of this multi-step theory is, at best, a hypothesis, unsupported by the scientific literature on which these experts rely. Further, what ***is*** presently known about ovarian cancer – including the fact that it is not one, but many, diseases with varying risk factors and etiologies – directly undermines plaintiffs' experts' speculative assumption that talc uniformly causes all types of ovarian cancers in the same way. Plaintiffs' arguments in response lack merit.

First, there is no truth to plaintiffs' suggestion that the J&J defendants improperly seek to hold plaintiffs' experts to a standard of "certainty" with respect to biological plausibility. As set forth in defendants' opening memorandum, and explained further below, the law is clear that expert opinions regarding biological plausibility cannot be based on a mere hypothesis. Instead, plaintiffs' experts must have some scientific evidence that the mechanism they propose actually works in the way they have theorized – evidence that is absent here. Plaintiffs' alternative argument that biological plausibility is not important to the evaluation of general

causation under a Bradford Hill analysis is similarly meritless. The identification of a biologically plausible mechanism by which an agent is capable of causing a disease is critical where the available epidemiological evidence demonstrates – at best – a very weak association between the agent and disease, and other Bradford Hill considerations are not satisfied.

Second, it simply is not true that plaintiffs' experts' failure to take account of the differences among the various subtypes of ovarian cancer is justified because defendants' experts similarly lump all ovarian cancers together. To the contrary, the J&J defendants' experts have expressly opined that, while the different subtypes of ovarian cancer are commonly referred to as a single disease, they are actually many diseases, with different hallmarks and origins, rendering any causation opinion that fails to differentiate between them unreliable. Further, while plaintiffs insist in their briefing that their experts did take the differences among the various subtypes of ovarian cancer into account, the reports and testimony of these experts do not bear that out.

Third, despite plaintiffs' protestations to the contrary, none of their experts has identified any reliable scientific evidence that actually supports their theory that particles of talc dusted ***externally*** on a woman's perineum enter the body, travel upward through the genital tract and lodge themselves in the ovaries and fallopian tubes. Instead, plaintiffs – like their experts – rely on factually dissimilar

studies demonstrating that large amounts of talc and other substances ***introduced directly into the vaginal cavities*** of animals and women – often in unnatural circumstances specifically designed to encourage the transport of particulates further into the body – can reach these organs. Plaintiffs' experts similarly lack support for their "secondary" theory that talc can be inhaled and transported to the ovaries through the lymphatic system, which is based entirely on speculation and contradicted by logic.

Fourth, plaintiffs similarly cannot refute that their experts' opinions regarding the mechanism by which talc purportedly causes cancer in the ovaries – i.e., chronic inflammation – is unsupported by the literature they cite. The simple fact is that neither plaintiffs nor their experts can point to any reliable, scientific evidence that talc causes ***chronic*** inflammation in human reproductive tissue. Nor can they identify even one study demonstrating that chronic inflammation is capable of triggering any – much less all – forms of ovarian cancer. Instead, plaintiffs' experts rely on literature suggesting that chronic inflammation may be associated with ***other*** types of cancer in ***other*** organs. But even plaintiffs admit that "different tissues react differently" to alleged carcinogens. And without some evidence that ovarian cancer, specifically, is caused by inflammation, their entire biological plausibility theory is nothing more than an unsupported hypothesis.

Finally, plaintiffs cannot deny that their expert Dr. Judith Zelikoff – who seeks to provide biological plausibility and other opinions – plagiarized significant portions of her report, inherently undermining the reliability of her methods and opinions. Instead, plaintiffs misleadingly attempt to downplay the extent of Dr. Zelikoff's plagiarism, which touches nearly every aspect of her report, including her ultimate conclusions.

For all of these reasons, plaintiffs' experts' biological plausibility opinions should be excluded.

ARGUMENT

I. PLAINTIFFS MISSTATE THE STANDARD BY WHICH THEIR EXPERTS' BIOLOGICAL PLAUSIBILITY OPINIONS MUST BE JUDGED.

As explained in defendants' opening brief, while *Daubert* does not require that a precise biological mechanism be conclusively established, "there still must be 'sufficiently compelling proof' of that mechanism" to show that it is a biologically plausible theory of causation.[1] This threshold requirement is critical because any number of hypothesized mechanisms might be ***theoretically possible***, but no mechanism can be deemed ***biologically plausible*** without a showing "that

[1] (Defs.' Mem. of Law in Supp. of Mot. to Exclude Pls.' Experts' Ops. Related to Biological Plausibility ("Defs.' Br.") at 6-7, May 7, 2019 (ECF No. 9736-1) (quoting *Soldo v. Sandoz Pharm. Corp.*, 244 F. Supp. 2d 434, 561-62 (W.D. Pa. 2003)).)

the allegedly dangerous substance 'behaves in the hypothesized way in the real world.'"[2]

In their response, plaintiffs do not address the significant amount of case law cited by the J&J defendants on this point. Instead, plaintiffs falsely assert that the J&J defendants have taken the position that conclusive proof of a biological mechanism is required.[3] In addition, plaintiffs offer the alternative argument that it does not matter whether their experts have reliable evidence to support their biological plausibility opinions because a showing of biological plausibility is "not required" to establish general causation.[4] Neither argument is valid.

First, plaintiffs' repeated insistence that a biological mechanism by which talc can cause cancer need not be proven ***conclusively*** is a point that no one disputes. But – as the long line of cases cited in the J&J defendants' opening brief make clear – it is well-recognized that a mere "hypothesis in need of further investigation" does not pass muster under *Daubert*. *Henricksen v. ConocoPhillips Co.*, 605 F. Supp. 2d 1142, 1175-76 (E.D. Wash. 2009).[5] Even the cases cited by plaintiffs are in accord. For example, in *Allison v. McGhan Medical Corp.*, 184

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[2] (*Id.* at 7 (quoting *In re Nexium (Esomeprazole) Prods. Liab. Litig.*, No. ML 12-2404 DSF (SSx), 2014 WL 5313871, at *3 (C.D. Cal. Sept. 30, 2014), *aff'd*, 662 F. App'x 528 (9th Cir. 2016)).)

[3] (Pls.' Opp'n at 5-8.)

[4] (*See id.* at 8-9.)

[5] (*See* Defs.' Br. at 6-9.)

F.3d 1300 (11th Cir. 1999), the Eleventh Circuit noted that "[w]hile scientific testimony need not be known to a certainty, *Daubert* does require that assertions be derived from 'scientific knowledge,'" which requires "more than subjective belief or unsupported speculation." *Id.* at 1319 n.23 (cited in Pls.' Opp'n at 7 n.14). Applying this standard, the Eleventh Circuit affirmed the district court's wholesale exclusion of an expert whose "hypothesis," like those at issue here, simply did "not have support in the scientific literature." *Id.* at 1318.

Plaintiffs' other cases are not to the contrary. For example, plaintiffs cite a recent district court opinion in *In re Abilify (Aripiprazole) Products Liability Litigation*, 299 F. Supp. 3d 1291 (N.D. Fla. 2018), for the proposition that "the PSC's experts 'need not prove the biological means by which [talcum powder] acts in the body.'"[6] But the opinion actually stated that experts "need not ***definitively*** prove the biological means by which a[n agent] acts in the body." 299 F. Supp. 3d at 1308 (emphasis added). Aside from silently omitting the key qualifying word from their quotation of this case, plaintiffs also ignore its holding. In *Abilify*, the court held that certain biological plausibility opinions were admissible because "[e]ach element of th[e] proposed mechanism of action [was] adequately supported by peer-reviewed, published scientific literature and sound scientific reasoning," while rejecting one biological plausibility opinion that "present[ed] an

[6] (Pls.' Opp'n at 7 (quoting 299 F. Supp. 3d at 1308).)

extrapolation problem," because the relevant studies examined medications that did not act on dopamine receptors in exactly the same way as those at issue in the litigation. *Id.* at 1342-44.[7]

As set forth below, plaintiffs' experts' biological plausibility opinions are inadmissible under this standard because they cannot point to any evidence that talc moves through the body to the ovaries in the way they propose – or that it causes the reactions they theorize. And plaintiffs' experts' attempt to extrapolate from studies involving exposures to different substances in very different circumstances or studies regarding the origins of different types of cancer is too attenuated to render their theories plausible.[8]

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[7] Plaintiffs cite a variety of other cases in which courts have admitted biological plausibility opinions based on a finding that they were appropriately supported by sufficient scientific evidence. (*See* Pls.' Opp'n at 7-8 (citing *In re Fosamax (Alendronate Sodium) Prods. Liab. Litig.*, Nos. 11-5304, 08-08, 2013 WL 1558697, at *6 (D.N.J. Apr. 11, 2013); *In re Roundup Prods. Liab. Litig.*, No. 16-md-02741-VC, 2018 WL 3368534, at *17 (N.D. Cal. July 10, 2018); *Karlo v. Pittsburgh Glass Works, LLC*, 849 F.3d 61, 81 (3d Cir. 2017); *In re Avandia Mktg., Sales Practices & Prods. Liab. Litig.*, No. 2007-MD-1871, 2011 WL 13576, at *9 (E.D. Pa. Jan. 4, 2011); and *Bartoli v. Novartis Pharm. Corp.*, No. 3:13-0724, 2014 WL 1515870, at *7 (M.D. Pa. Apr. 17, 2014)).) But as set forth in detail in the J&J defendants' opening brief and below, plaintiffs here lack any reliable scientific evidence capable of showing that the hypothesized biological mechanism they propose actually works in the real world.

[8] Plaintiffs' suggestion that the Court should simply let the jury decide whether the relevant science provides sufficient support for expert opinions similarly misstates the law. It is axiomatic that "the centerpiece of the *Daubert* regime is the gatekeeping role of the trial judge, whose duty it is to screen challenged expert testimony and assure that it is sufficiently reliable to be of

Second, plaintiffs' alternative argument, which attempts to minimize the significance of biological plausibility under the Bradford Hill framework, is similarly meritless. Plaintiffs cite Bradford Hill's statement that biological plausibility is "a feature I am convinced we cannot demand" in every case.[9] But the context for that statement was the ***200-fold*** increase in scrotum cancer for late-18th and early-19th century chimney sweeps. We are no longer in the 19th century, when nothing was known about cancer, and the association here is weak and inconsistent. Under these circumstances, it is essential that plaintiffs be able to demonstrate the biological plausibility of their causation theory.[10] *See In re Mirena IUS Levonorgestrel-Related Prods. Liab. Litig. (No. II)*, 341 F. Supp. 3d 213, 286 (S.D.N.Y. 2018) (holding that where "scholarship has *not* shown more than a correlation, subject to identifiable confounders, between [the product and the disease]," "it is not enough" "for an expert as to general causation to opine that a biological pathway exists but is not well understood"). Indeed, to the extent

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assistance to the jury." *Asplundh Mfg. Div., a Div. of Asplundh Tree Expert Co. v. Benton Harbor Eng'g*, 57 F.3d 1190, 1202 (3d Cir. 1995).

9 (Pls.' Opp'n at 8.)

10 *See, e.g.*, Wynder et al., Weak Associations in Epidemiology and Their Interpretation, 11 Preventive Med. 464, 465 (1982) (attached as Ex. A157 to Certification of Julie L. Tersigni ("Tersigni Cert."), May 7, 2019 (ECF No. 9723-2)) ("Because chance or bias can easily produce a spurious weak association, the need to seek supporting evidence is greater with weak than with strong associations.").

biological plausibility is not relevant here, that is because, as defense expert Dr. Christian Merlo opined, the other Hill criteria are not satisfied and biological plausibility alone cannot demonstrate causation.[11]

In short, plaintiffs' attempt to downplay their experts' burden to support their speculative biological plausibility opinions with relevant scientific evidence is inconsistent with the law and good science.

II. PLAINTIFFS' EXPERTS' BIOLOGICAL PLAUSIBILITY THEORIES ARE INHERENTLY UNRELIABLE BECAUSE THEY DO NOT ACCOUNT FOR THE FACT THAT THERE ARE SEVERAL SUBTYPES OF OVARIAN CANCER WITH DIFFERENT ETIOLOGIES.

As explained in defendants' opening brief, an overarching problem with all of plaintiffs' experts' biological plausibility opinions is the fact that they fail to adequately account for the undisputed fact that ovarian cancer is ***not*** a single disease, but instead includes a variety of distinct diseases that involve mutations of different genes, develop in different tissues and have different risk factors and etiologies.[12] Disregarding this established principle, plaintiffs' experts improperly lump all ovarian cancers together, mixing data pertaining to different subtypes in order to opine that there is a biological mechanism by which talc causes all types

[11] (*See* Dep. of Christian Merlo, M.D., M.P.H. 178:24-179:5, Apr. 18, 2019 (attached as Ex. B9 to Tersigni Cert.) ("[W]ith a lack of strength of association, with a lack of consistency between studies and with a lack of dose response, biologic plausibility doesn't matter because there's no causal association between talcum powder and ovarian cancer based on the medical literature.").)

[12] (*See* Defs.' Br. at 9-18.)

of ovarian cancers uniformly.[13] In attempting to defend their experts, plaintiffs argue that: (1) the scientific community treats ovarian cancer as a single disease because there are "many commonalties" among the subtypes; and (2) their experts did consider and evaluate the various subtypes of ovarian cancer in forming their biological plausibility opinions.[14] Both arguments should be rejected.

First, plaintiffs' assertion that the scientific community – including defense experts – "often refer to epithelial ovarian cancer as one disease" because of "similarities, particularly with respect to etiology," is untrue.[15] Notably, plaintiffs are unable to cite even one statement by any defense expert in support of this proposition. This is unsurprising because, while the J&J defendants' experts use the shorthand term "ovarian cancer" to reference all subtypes of the disease in general contexts, they have made very clear in their reports and testimony that the different subtypes are distinct, especially with respect to their etiologies and risk factors, rendering any causation opinion that conflates them inherently unreliable.[16]

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13 (*Id*.)

14 (Pls.' Opp'n at 3, 32.)

15 (*Id*. at 3.)

16 (*See, e.g.*, Expert Report of Benjamin G. Neel, M.D., Ph.D. ("Neel Rep.") at 12, Feb. 25, 2019 (attached as Ex. C10 to Tersigni Cert.) ("Taken together, these findings clearly show that different types of ovarian cancer originate in different cell types that suffer different types of mutations, which are unlikely to be caused by the same environmental agent. *Studies, including epidemiological reports, that treat 'ovarian cancer' as a single entity, should, in my opinion, be viewed with skepticism.*"); Expert Report of Ie-Ming Shih, M.D., Ph.D. ("Shih Rep.") at 13,

Nor is it true that the scientific community has accepted that all ovarian cancer subtypes can be lumped together when evaluating etiology or causation. To the contrary, the published literature has made clear that "[a]nalyses ***not*** taking into account differences in ovarian cancer risk by histologic subtype could be misleading" due to the variations among these conditions and their origins.[17] Indeed, even plaintiffs' own experts concede that, in analyzing causation "it is

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Feb. 25, 2019 (attached as Ex. C20 to Tersigni Cert.) (criticizing epidemiological studies that "apparently lumped all types of ovarian cancer together in their analyses" because "various types of ovarian cancer are characterized by distinct clinicopathological and molecular features" and "their origins and risk factors are all different"); Expert Report of Karla Ballman, Ph.D. at 39, Feb. 25, 2019 (attached as Ex. C25 to Tersigni Cert.) ("[G]iven that ovarian cancer has several subtypes that are often researched as separate diseases and may well have different causes, there is no coherence to the extent plaintiffs' experts contend that perineal talc use increases the risk of multiple subtypes of ovarian cancer."); Kurman Rep. at 2-3 (asserting that "[i]t is hard to imagine that exposure to talcum powder could cause the development of all of these unique histological subtypes of EOC" and pointing out that "even the epidemiology studies that report a weak statistically significant increased risk for talcum powder users have inconsistent results when broken down by histological subtype").)

[17] Gates et al., *Risk Factors for Epithelial Ovarian Cancer by Histologic Subtype*, 171(1) Am J Epidemiol. 45, 52 (2010) (attached as Ex. A42 to Tersigni Cert.) (emphasis added); *see also* Zorn et al., *Gene Expression Profiles of Serous, Endometrioid, and Clear Cell Subtypes of Ovarian and Endometrial Cancer*, 11(18) Clinical Cancer Res. 6422, 6422 (abstract) (2005) (attached as Ex. A197 to 2d Suppl. Certification of Julie L. Tersigni ("2d Suppl. Tersigni Cert.")) ("The comparison of the gene expression profiles of endometrioid and serous subtypes of ovarian and endometrial cancer are largely unique to the combination of a particular subtype in a specific organ.").

important to identify, at the minimum, the type of cancer, stage of cancer at diagnosis, and subtype of cancer."[18]

Plaintiffs cite three studies for the proposition that all epithelial ovarian cancer subtypes have similar "causal factors such as inflammation" and therefore may be treated as a "single disease,"[19] but none supports this proposition. For example, Balkwill (2001) only mentions ovarian cancer once, in a chart, and does not contain any discussion of purported similarities among the various subtypes of ovarian cancer.[20] The Shan (2009) paper cited by plaintiffs similarly contains no analysis of whether the different subtypes of ovarian cancer are similar or may be

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[18] (Expert Report of Anne McTiernan, M.D., Ph.D. ("McTiernan Rep.") at 17, Nov. 16, 2018 (attached as Ex. C7 to Tersigni Cert.); *see also* Expert Report of Rebecca Smith-Bindman, M.D. ("Smith-Bindman Rep.") at 9, Nov. 15, 2018 (attached as Ex. C36 to Tersigni Cert.) ("Ovarian cancers . . . are a heterogeneous group of malignancies that vary in their pathological appearance, molecular biology, risk factors, etiology, and prognosis."); Smith-Bindman Rep. at 9 ("Understanding ovarian cancer histologic types is important because the risk factors, etiology and genetics of ovarian cancer can vary by histological type. Therefore, the importance of talcum powder products as a risk factor or cause can also vary by type.").)

[19] (Pls.' Opp'n at 32 n.88 (citing Savant et al., *The Role of Inflammation and Inflammatory Mediators in the Development, Progression, Metastasis, and Chemoresistance of Epithelial Ovarian Cancer*, 10(8) Cancers 251, at 2 (2018) ("Savant 2018") (attached as Ex. 76 to Pls.' Opp'n); Shan & Liu, *Inflammation: A Hidden Path to Breaking the Spell on Ovarian Cancer*, 8(19) Cell Cycle 3107, 3108 (2009) ("Shan 2009") (attached as Ex. 80 to Pls.' Opp'n); and Balkwill & Mantovani, *Inflammation and Cancer: Back to Virchow?*, 357 Lancet 539, 539 (2001) ("Balkwill 2001") (attached as Ex. 61 to Pls.' Opp'n)).)

[20] Balkwill 2001 at 539.

conflated for purposes of assessing causation.[21] And in Savant (2018) – an article not discussed in any of the reports submitted by plaintiffs' experts – the authors specifically recognized that there are different subtypes of epithelial ovarian cancer and focused their analysis of inflammation as a risk factor on just one of those subtypes.[22] In short, plaintiffs cannot point to any scientific literature suggesting that all ovarian cancer subtypes have similar origins. Rather, as explained in defendants' opening brief, all of the available evidence shows otherwise.[23]

Second, plaintiffs' alternative argument that their experts ***did*** analyze the different subtypes of epithelial ovarian cancers in forming their biological plausibility opinions fares no better.[24] For one thing, plaintiffs make no attempt to point to any evidence that Drs. Carson, Kane, Plunkett or Singh mentioned, much less considered, the variations in ovarian cancer subtypes in reaching their opinions. And the portions of the reports of Drs. Zelikoff and McTiernan cited by plaintiffs merely mention in passing that there are different subtypes of ovarian cancer, with no explanation of their differences or similarities.[25] Indeed, Dr. Zelikoff expressly

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21 Shan 2009 at 3107-11.

22 Savant 2018 at 2.

23 (Defs.' Br. at 9-13.)

24 (*See* Pls.' Opp'n at 33.)

25 (*See, e.g.*, Expert Report of Judith Zelikoff, Ph.D. ("Zelikoff Rep.") at 19 , Nov. 16, 2018 (attached as Ex. C24 to Tersigni Cert.) ("Ovarian cancer comprises at least five distinct histological subtypes, the most common and well-studied being high-grade serous ovarian cancer."); McTiernan Rep. at 17 ("There are

admitted at her deposition that she ***did not*** consider whether or how her theory of biological plausibility applied to these different subtypes of the disease.[26] And other experts summarily dismiss the differences among the various subtypes without any scientific support or explanation as to why these differences are irrelevant to their theories of biological plausibility.[27]

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several different subtypes of cancer of the ovary."); Expert Report of Patricia G. Moorman, MSPH, Ph.D. ("Moorman Rep.") at 29, Nov. 16, 2018 (attached as Ex. C35 to Tersigni Cert.) ("[T]he most recent meta-analysis did report statistically significant associations with invasive serous ovarian cancer in the cohort studies as well as in the case-control studies that reported on histologic subtype.").)

[26] (Dep. of Judith Zelikoff, Ph.D., Jan. 21, 2019 ("Zelikoff Dep.") 193:11-14 (attached as Ex. B31 to Tersigni Cert.).)

[27] (*See, e.g.*, Expert Report of Daniel L. Clarke-Pearson ("Clarke-Pearson Rep.") at 3, Nov. 16, 2018 (attached as Ex. C14 to Tersigni Cert.) ("[W]e believe that EOC, fallopian tube carcinoma and primary peritoneal carcinoma are the same entity and share similar risk factors and pathogenesis."); Expert Report of Jack Siemiatycki MSc, Ph.D.("Siemiatycki Rep.") at 47, Nov. 16, 2018 (attached as Ex. C21 to Tersigni Cert.) ("[T]here is no persuasive evidence in these studies, taken as a whole that the effect of talc differs by histologic subtype of epithelial ovarian cancer."); Expert Report of Ellen Blair Smith, M.D. ("Smith Rep.") at 2-3, Nov. 16, 2018 (attached as Ex. C16 to Tersigni Cert.) ("For our purposes, we consider epithelial cancers of the ovary, fallopian tubes, and peritoneum to be a single entity."); Expert Report of Judith Wolf, M.D. ("Wolf Rep.") at 3, Nov. 16, 2018 (attached as Ex. C23 to Tersigni Cert.) ("Epithelial carcinoma of the ovary, fallopian tube, and peritoneum are usually considered as a single entity due to their common clinical behavior, risk factors, and pathogenesis."); Dep. of Shawn Levy 259:4-260:8, Jan. 11, 2018 (attached as Ex. B46 to Tersigni Cert.) (offering the unsupported opinion that the mechanism of cancer is not exclusive to any one type).) While Dr. Smith-Bindman includes a background discussion that highlights the different subtypes of epithelial ovarian cancer and even acknowledges that the subtypes "vary in their pathological appearance, molecular biology, risk factors, etiology and prognosis," she proceeds to abandon this knowledge in her discussion of inflammation, in which she treats inflammation as

In sum, plaintiffs' experts' failure to grapple with the fundamental differences among ovarian cancer subtypes makes their opinions unreliable.

III. PLAINTIFFS' EXPERTS LACK RELIABLE EVIDENCE SUPPORTING THE HYPOTHESIS THAT TALC APPLIED EXTERNALLY CAN REACH THE FALLOPIAN TUBES OR OVARIES.

Plaintiffs also cannot refute defendants' argument that their experts' biological plausibility opinions are unreliable because they lack scientific evidence supporting the very first link in the chain of their tenuous causation hypothesis – that ***externally-applied*** talc reaches the fallopian tubes and ovaries, either by: (1) migrating through the genital tract; or (2) being inhaled and moving through the entire lymphatic system, which even plaintiffs describe as only a potential "secondary" route.[28]

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the cause of essentially all cancer and fails to mention the subtypes of epithelial ovarian cancer or address whether inflammation is the posited cause of one, some or all of them. (*See* Smith-Bindman Rep. at 9, 12-13.)

[28] More than a dozen of plaintiffs' experts offer opinions on these topics. (*See* Expert Report of Ghassan Saed, Ph.D. ("Saed Rep.") at 11-12, Nov. 16, 2018 (attached as Ex. C17 to Tersigni Cert.); Zelikoff Rep. at 12-14; Expert Report of Sarah E. Kane, M.D. ("Kane Rep.") at 4, 14, Nov. 15, 2018 (attached as Ex. C38 to Tersigni Cert.); Wolf Rep. at 11; Smith Rep. at 16-17; Smith-Bindman Rep. at 35; Clarke-Pearson Rep. at 7-8; Moorman Rep. at 33; Expert Report of Laura M. Plunkett, Ph.D., DABT ("Plunkett Rep.") at 27-38, Nov. 16, 2018 (attached as Ex. C28 to Tersigni Cert.); McTiernan Rep. at 8, 58-63, 66; Expert Report of Arch Carson, M.D., Ph.D. ("Carson Rep.") at 7-8, Nov. 16, 2018 (attached as Ex. C9 to Tersigni Cert.); Siemiatycki Rep. at 30, 65; Expert Report of Sonal Singh, M.D., M.P.H. ("Singh Rep.") at 18-19, 57, Nov. 16, 2018 (attached as Ex. C40 to Tersigni Cert.).)

A. Plaintiffs' Experts Lack Reliable Evidence That Externally-Applied Talc Migrates Inside The Body And Up To The Ovaries Or Fallopian Tubes.

Plaintiffs' experts seek to opine that it is biologically plausible that talc dusted externally on a woman's perineum in day-to-day use can enter the body and travel, against gravity, up the vagina, through the cervix, past the uterus and embed in the fallopian tubes and ovaries – all in amounts sufficient to cause an inflammatory reaction that plaintiffs' experts insist is capable of causing cancer. As explained in the J&J defendants' opening brief, the problem with these opinions is that ***none*** of the evidence on which plaintiffs' experts rely comes anywhere close to suggesting that this is a plausible scenario.[29]

In their opposition, plaintiffs suggest that the J&J defendants' criticisms of their experts' migration opinions merely "parse[] out individual studies [relied on by the experts] and critiqu[e] . . . some" of them.[30] In truth, the J&J defendants have explained that plaintiffs' experts are ***unable to point to even one study*** demonstrating (or even suggesting) that externally dusted talc (or any other substance) can make it to the ovaries from the perineum. Instead, the experts rely on: (1) pathological evidence that talc can be found in the ovaries of women ***regardless of whether they engage in perineal talc use***; (2) studies involving entirely inapposite circumstances of exposure, in which large quantities of talc and

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29 (*See* Defs.' Br. at 18-40.)

30 (Pls.' Opp'n at 34-35.)

other substances are directly inserted into the vaginas (or higher locations in the genital tract) of women, often in manipulated environments specifically designed to encourage the flow of particulates into the body; and (3) animal studies that almost exclusively involve forced internal application of particulates and – in any event – demonstrate little, if anything, about the movement of those particulates through the anatomically-distinct human genital tract. None of these publications, on their own or taken together, supports the notion that it is biologically plausible that a woman who dusts the outside of her body will have talc particles ascend to the ovaries and cause cancer there.

1. Limited Evidence Of Talc In Reproductive Tissue Does Not Make Migration From The Perineum Plausible.

Plaintiffs' experts rely on three studies in which researchers purported to identify talc particles in tissue taken from the reproductive tracts of human patients, including the ovaries and lymph nodes. But, as the J&J defendants explained in their opening brief, not one of these studies comes anywhere close to supporting plaintiffs' experts' conclusions that talcum powder ***applied to the perineum*** may be absorbed into the vagina and migrate to the tubes and ovaries.[31]

Plaintiffs are forced to concede in their opposition brief that, at most, "these studies only prove that talc got to the ovaries and lymph nodes from somewhere" because there is no indication that the talc identified originated and migrated from

[31] (*See* Defs.' Br. at 20-24.)

the perineum.[32] Plaintiffs argue, however, that "when viewed through the lens of the totality of the evidence on the ability of particles to migrate upward from the vagina," the "presence of talc in the ovaries and lymph nodes" has "scientific significance."[33] The problem with this argument is that, as explained in detail below, plaintiffs' experts have ***zero*** evidence that cosmetic talc applied ***externally*** to the perineum migrates upward through the genital tract – let alone that it can do so in the quantities necessary for the remainder of plaintiffs' experts' theories to be plausible. Further, as the J&J defendants explained in their opening brief, one of the studies plaintiffs' experts cite as demonstrating that talc can be found in ovarian tissue – Heller (1996) – observed talc in the tissue of ***both*** women who used cosmetic talc externally ***and those who did not***.[34] Thus, if anything, the study indicates that perineal talc use was ***not*** the source of the talc particles that were identified.[35]

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32 (Pls.' Opp'n at 35.)

33 (*Id*. at 35-36.)

34 (Defs.' Br. at 22.)

35 Plaintiffs claim that the J&J defendants "ignore[d]" a different study by Heller, which they claim "demonstrated the presence of asbestos in ovarian tissue and concluded that 'women with a positive [asbestos] exposure history had asbestos detected in their ovaries more frequently.'" (Pls.' Opp'n at 36 n.95 (quoting Heller et al., *Asbestos Exposure and Ovarian Fiber Burden*, 29 Am. J. Indus. Med. 434, 439 (1996) ("Heller (1996) – Asbestos") (attached as Ex. A59 to Tersigni Cert.)).) This is untrue. As the J&J defendants explained in their opening brief, Heller's asbestos study is entirely irrelevant because the presence of asbestos in ovarian tissue says nothing about ***talc*** or whether it can reach the ovaries or

In addition to the studies relied upon by their experts, plaintiffs point to McDonald (2019), which plaintiffs claim "confirmed . . . 'that talc particles, from perineal exposure, can and do migrate to pelvic lymph nodes.'"[36] But, as the J&J defendants explained in their opening brief, that study was authored by other plaintiffs' experts in the talc litigation and did not identify any talc in tissue from the ***ovaries or fallopian tubes***.[37] Further, while the authors concluded that they found particles in the lymphatic system that were "likely to be talc," they also conceded that some of the particles identified were "likely nonspecific particulate material which finds its way into the perineum through general living and hygiene practices," as opposed to talc.[38] Thus, it is not clear how much – if any – talc was actually identified or what the source of that talc was.

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fallopian tubes. (Defs.' Br. at 22 n.46.) This is especially true because that study did not involve women who reported dusting asbestos externally on their perineums and therefore says nothing about whether ***any*** particulate applied in that manner can reach the internal organs. In any event, as explained in Defendants' Reply in Support of Motion to Exclude Plaintiffs' Experts' Asbestos-Related Opinions, Heller found significant asbestos burdens in six of 17 women with no known exposure to asbestos.

[36] (Pls.' Opp'n at 36-37 (quoting McDonald et al., *Correlative polarizing light and scanning electron microscopy for the assessment of talc in pelvic region lymph nodes*, 43 Ultrastructural Pathol. 1, 12 (2019) ("McDonald 2019") (attached as Ex. A93 to Tersigni Cert.)).)

[37] (Defs.' Br. at 21 n.44.)

[38] (*Id*. (quoting McDonald 2019 at 2).)

Plaintiffs incorrectly assert that "J&J's only critique of the[] studies" relied upon by plaintiffs' experts is that the talc identified in them "came from contamination."[39] As set forth above, however, that is not the case. The primary problem with plaintiffs' reliance on these studies is that there is no scientific basis to conclude that the talc purportedly identified therein originated from genital talc use and not some other source, whether it be talc in food, some other source or laboratory contamination.[40] Further, plaintiffs cannot dispute that even the Cramer and McDonald studies on which they heavily rely expressly note the possibility of contamination and concede that it is a likely explanation for the findings of talc in the tissue of both exposed and unexposed patients observed in Heller (1996).[41]

2. Human Studies Do Not Support Plaintiffs' Experts' Migration Opinions.

Plaintiffs are also unable to refute that the experimental human studies on which their experts rely do not support the biological plausibility of their migration opinions because none of them demonstrates that ***externally-dusted*** cosmetic talc

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39 (Pls.' Opp'n at 36.)

40 (*See* Dep. of Brooke T. Mossman, M.S., Ph.D. 348:17-349:10, Apr. 8, 2019 (attached as Ex. B7 to Tersigni Cert.) (noting that talc observed in human tissue may have originated from a variety of sources given that "[t]alc is in a lot of different food processes" and "plastics" and therefore "[w]e're all exposed to it").)

41 *See* McDonald 2019 at 7 tbl. 1, 12.; Cramer et al., *Presence of Talc in Pelvic Lymph Nodes of a Woman with Ovarian Cancer and Long-Term Genital Exposure to Cosmetic Talc*, 110(2) Obstet Gynecol. 498, 500 (2007) (attached as Ex. A24 to Tersigni Cert.).

is capable of making its way to the ovaries or fallopian tubes.[42] Instead, each of the cited studies involved the internal application of large amounts of particulates – not limited to talc – far within the genital tract, often in circumstances that were specifically designed to encourage upward motility toward the ovaries and fallopian tubes.[43] Plaintiffs' arguments in response lack merit.

First, plaintiffs contend that "real life and the female anatomy" indicate that talc dusted on the perineum necessarily makes it into the vagina because "women exercise, use the restroom, use tampons, lay down [sic], and engage in sexual intercourse" and therefore, "the outside world has access to the peritoneal cavity through the vagina."[44] But none of plaintiffs' experts mentions activities such as exercise, using tampons, using the restroom, lying down or sexual intercourse in their reports as plausible mechanisms by which externally-applied talc can be introduced into the upper genital tract. *See In re Rezulin Prods. Liab. Litig.*, 369 F. Supp. 2d 398, 407 (S.D.N.Y. 2005) (rejecting plaintiffs' counsel's attempts to defend expert opinions by "form[ing] hypotheses that the experts nowhere mentioned" and "forg[ing] connections that the experts stopped short of drawing" because the subject of a *Daubert* "motion is the proposed testimony of experts, not the theories of the lawyers"). Nor do the scientific authorities plaintiffs' counsel

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42 (*See* Defs.' Br. at 25-32.)

43 (*Id.*)

44 (Pls.' Opp'n at 38.)

cite in their briefing support the notion that such day-to-day activities cause the uninhibited flow of particulates deep into the vaginal cavity. Indeed, while plaintiffs quote selectively from Huncharek et al. (2007) for this proposition, the article states the opposite. As the authors explain:

> Although ***in the experimental setting*** translocation of talc particles [from the vagina] to the human ovary can occur with ***deliberate or inadvertent manipulations of patients*** in the supine position (Wehner, 1998), it is unknown whether cosmetic use of talc in the perineal area can routinely penetrate the female reproductive tract and reach the ovary against physiological forces working in the opposite direction.[45]

Notably, even if plaintiffs or their experts had evidence that activities like lying down and going to the bathroom are capable of introducing externally-applied particulates into the vagina, there certainly is no evidence that it would be in amounts anywhere close to the volume of talc inserted into the upper genital tracts of the participants in the studies on which plaintiffs rely.[46] Nor do plaintiffs'

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[45] Huncharek et al., *Use of Cosmetic Talc on Contraceptive Diaphragms and Risk of Ovarian Cancer: A Meta-Analysis of Nine Observational Studies*, 16(5) Eur J Cancer Prev. 422, 423 (2007) (attached as Ex. A68 to Tersigni Cert.) (emphases added). Plaintiffs also rely on Heller's 1996 asbestos article, which – as discussed above – addressed findings of asbestos, not talc, in reproductive tissue. The Heller asbestos article provides no evidence with respect to the migration of particles form the perineum. Indeed, the portion of the article that plaintiffs cite addresses incidences of ***mesothelioma*** among women with secondary exposure to occupational asbestos through a spouse and merely notes that because the data indicate that "exposure to a husband is more significant than exposure to a father," there is a "possible role for sexual contact as a transporting vector for asbestos fiber" to the lungs. Heller (1996) – Asbestos at 438.

[46] Nor do any of the other studies cited by plaintiffs support their assertion that "the outside world has access to the peritoneal cavity through the vagina, uterus

experts cite any evidence that occasional, episodic introduction of talc particles into the vagina during, for example, sexual intercourse or the use of tampons is capable of causing cancer. To the contrary, plaintiffs' experts admit that studies evaluating whether a statistically significant association exists between the

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and fallopian tube." (Pls.' Opp'n at 38 (citing Folkins et al., *Assessing Pelvic Epithelial Cancer Risk and Intercepting Early Malignancy*, in *Diagnostic Gynecologic and Obstetric Pathology* 846 (3d ed. 2017) ("Folkins 2017") (attached as Ex. 32 to Pls.' Opp'n); Houghton et al., *Perineal Powder Use and Risk of Ovarian Cancer*, 106 JNCI 1, 1 (2014) ("Houghton 2014") (attached as Ex. A65 to Tersigni Cert.); and Langseth et al., *Perineal Use of Talc and Risk of Ovarian Cancer*, 62 J. Epidemiol. Comm. Health 358, 358 (2008) ("Langseth 2008") (attached as Ex. A88 to Tersigni Cert.)).) Folkins is merely a chapter of a textbook that describes the "ascending carcinogen hypothesis" but does not provide any primary data for plaintiffs' migration theory. Folkins 2017 at 846. And while Houghton posits that talc has "been shown to migrate to the ovaries," Houghton 2014 at 1, the only citation for that proposition – Muscat and Huncharek – not only does not support Houghton's point but expressly casts doubt on whether the migration hypothesis has any support at all. *See* Muscat & Huncharek, *Perineal Talc Use and Ovarian Cancer: A Critical Review*, 17 Eur J Cancer Prev. 139, 142 (2008) (attached as Ex. A192 to 2d Suppl. Tersigni Cert.) (explaining that "an exposure route [for talc] on the basis of perineal dusting requires unproven assumptions about vaginal exposure"). Likewise, Langseth merely notes the occurrence of retrograde menstruation and the purportedly protective effect of tubal ligation against ovarian cancer – neither of which has anything to do with the ability of an externally-applied talc particle to travel through the vaginal tract. (*See* Expert Report of Michael Birrer, M.D., Ph.D. ("Birrer Rep.") at 10, Feb. 25, 2019 (attached as Ex. C33 to Tersigni Cert.) (retrograde menstruation "occurs more closely to the fallopian tubes than does perineal dusting, and it may be facilitated by uterine contractions that would not be occurring in the ordinary course during perineal dusting"); Defs.' Mem. of Law. in Opp'n to Pls.' Mot. to Exclude the Ops. of Robert Kurman, M.D. at 20 & n.51, May 29, 2019 (ECF No. 9872) (explaining that compositional and functional changes in the tubal fimbriated ends – and not any protection from the purported effects of migration of environmental toxins – explains why tubal ligation reduces the risk of high grade serous carcinoma).)

episodic use of talc-dusted diaphragms and condoms (which would place talc directly against a woman's cervix) and ovarian cancer have concluded that it does not.[47]

Second, plaintiffs assert that "the evidence is overwhelming that once in the vagina, particles rapidly migrate upward toward the ovaries and fallopian tubes."[48] But, as the J&J defendants explained in detail in their opening brief, the specific studies plaintiffs cite for this proposition involved manufactured conditions specifically designed to encourage the movement of particulates up the genital tract toward the ovaries, including the use of oxytocin, a drug that induces muscular contractions.[49] In response, plaintiffs focus on a single study – Sjösten et al. (2004) – which they claim observed the movement of cornstarch particulates from the vagina into the fallopian tubes without steps having been "taken to influence migration"[50] But, as the J&J defendants have explained, that study involved cornstarch deposited through gynecological examination, where the examiner may introduce the particles into the cervix with considerable force. Thus, the

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47 (*See, e.g.*, Dep. of Rebecca Smith-Bindman, M.D. Vol. II 271:6-10, Feb. 8, 2019 (attached as Ex. B42 to Tersigni Cert.); Dep. of Sonal Singh, M.D., MPH ("Singh Dep.") 167:3-8, Jan. 16, 2019 (attached as Ex. B47 to Tersigni Cert.); Dep. of Judith K. Wolf, M.D. 195:22-196:14, Jan. 7, 2019 (attached as Ex. B30 to Tersigni Cert.).)

48 (Pls.' Opp'n at 39.)

49 (*See* Defs.' Br. at 29-30.)

50 (Pls.' Opp'n at 39-40.)

circumstances of exposure are in no way analogous to the external dusting of the perineum with talc. Plaintiffs also suggest that the use of oxytocin and other artificial methods to encourage migration does not render the human studies inapposite because of "uterine peristalsis" – i.e. "rhythmic contractions in the female genital tract that occur regularly through a woman's menstrual cycle."[51] Yet, plaintiffs are unable to point to any literature suggesting that peristalsis results in contractions that are similar to those induced by oxytocin. And in any event, the primary study plaintiffs cite for the proposition that uterine peristaltic contractions can foster the retrograde migration of inert particles such as talc – Kunz (1997) – involved the placement of albumin spheres directly into the orifice "of the uterine cervix."[52] Thus, neither this study – nor any other cited by plaintiffs' experts – constitutes evidence that it is biologically plausible that peristaltic contractions can aid the upward migration of talc dusted externally on the perineum.

Third, plaintiffs assert – without citing any support – that it is of no matter that many of the human studies on which their experts rely involve the direct application of particles ***other than talc*** into the reproductive system because "all

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[51] (*Id.* at 10-12; *see also id.* at 39.)

[52] (Defs.' Br. at 27 (quoting Kunz et al., *The Uterine Peristaltic Pump: Normal and Impeded Sperm Transport within the Female Genital Tract, in* The Fate of the Male Germ Cell 267, 270 (Ivell & Holstein eds. 1997)).)

different types of particles . . . behave the same."[53] This is sheer speculation, however, which is not supported by scientific evidence. *See, e.g., Trivitis, Inc. v. Ocean Spray Cranberries, Inc.*, No. 10cv0316 JM (MDD), 2012 WL 1944827, at *5 (S.D. Cal. May 29, 2012) (plaintiff's "conclusory statements without citation to the record" in its *Daubert* opposition were improper; "[w]ithout specific citation to an evidentiary basis for these statements, [plaintiff] simply fails to carry its burden"); *Wright v. Case Corp.*, No. Civ.A. 1:03CV1618-JEC, 2006 WL 278384, at *5 (N.D. Ga. Feb. 1, 2006) (plaintiff's general assertions in his *Daubert* opposition, without citation to the record, were "insufficient to meet plaintiff's burden, as the proponent of expert testimony, to establish the reliability" of his expert's opinion).

3. Animal Studies Do Not Offer Reliable Evidence Of Migration.

Animal studies exploring the movement of particles forcibly applied to the genital tracts of rats, rabbits or other animals also are insufficient to render plaintiffs' experts' migration opinions biologically plausible. Indeed, plaintiffs admit as much, insisting that their experts rely on the human data for the migration opinions, "not on the handful of animal studies" they cite.[54] This is unsurprising given that some of plaintiffs' own experts have acknowledged that there are animal

53 (Pls.' Opp'n at 40.)

54 (Pls.' Opp'n at 41.)

data that directly undermine the theory that talc can migrate from the perineum to the ovaries.[55]

Nevertheless, plaintiffs attempt to defend their experts' reliance on animal studies, arguing that the cases cited by the J&J defendants – which hold that such studies have limited, if any, applicability in determining causation with respect to humans – are inapposite because they all involved "situations where the experts relied solely on animal studies and were unable to explain how the results from those studies were appropriately extrapolated to humans."[56] But, just as in those cases, none of plaintiffs' experts analyzes the significant differences between the reproductive tracts of human women and those of the rats, rodents and other small animals that are the subjects of the studies they cite.[57]

Further, it is simply untrue that courts have only questioned expert reliance on animal studies where they constituted the sole basis of the experts' opinions. For example, in *In re Rezulin*, 369 F. Supp. 2d 398 (cited in Defs.' Br. at 35), the court excluded expert opinions that the diabetes drug Rezulin could cause liver cell

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55 (*See* Carson Rep. at 7 (admitting there are "animal studies suggesting that this transport does not occur"); Singh Rep. at 18-19 (quoting Wehner et al., *On Talc Translocation From the Vagina to the Oviducts and Beyond*, 24(4) Food Chem Toxicol. 329, 331 (1986) ("Wehner 1986") (attached as Ex. A149 to Tersigni Cert.)) (acknowledging animal study that "failed to detect translocation of 'measurable quantities of talc'" placed in the vaginal tracts of moneys).)

56 (Pls.' Opp'n at 41.)

57 (Defs.' Br. at 32-35.)

death, because the opinions were premised on insufficiently analogous *in vivo* and *in vitro* studies. With respect to the animal studies, the court noted that they involved "different species [with] important physiological differences" and that the "high doses often used in animal studies may not correspond to considerably lower concentrations of a drug or other substance to which humans are in reality exposed." *Id*. at 407. In particular, the court noted that there was "no reason to believe that the doses used in" the animal study at issue in *Rezulin* "approximated the doses to which clinically relevant quantities of cells in the human liver are exposed." *Id*. at 438.

As explained in detail in the J&J defendants' opening brief, the same is true here. The animal studies relied on by plaintiffs' experts generally involve the introduction of overwhelming amounts of particles directly into the bodies – in most studies, the vagina or even the uterus – of rodents and other small mammals and therefore do not replicate the external dusting of talc on the perineum of a human woman.[58] Moreover, in many of the studies, even if some migration was

[58] (Defs.' Br. at 38-39.) As defendants have noted, the only animal study cited by plaintiffs' experts to support their migration opinions that involved external talc application was Keskin (2009), in which rats were forcibly sprayed with aerosolized talc in doses of 400mg/kg of body weight – the equivalent of a 132-pound woman using well more than half a travel-sized bottle per day. (*Id*. at 39-40.) And while that study purported to identify infection in the rat ovaries after exposure (as well as in one unexposed rat in the control group), it did not observe neoplastic changes, and it was unclear whether the talc itself had made its way to the rats' ovaries. (*Id*.)

shown, talc did not reach the ovaries or fallopian tubes.[59] Plaintiffs do not dispute this.

Plaintiffs also accuse the J&J defendants of incorrectly stating that many of plaintiffs' experts failed to consider the animal study with the most biological relevance to humans – Wehner (1986) – which studied primates instead of rodents and directly undermines plaintiffs' migration hypothesis.[60] While plaintiffs assert that their experts "did consider Wehner (1986) with the totality of the evidence," they essentially concede – as noted in the J&J defendants' briefing – that only three of the five experts who rely on animal studies as support for their migration opinions addressed Wehner in any way.[61] And plaintiffs cannot refute that those plaintiffs' experts who did mention Wehner in their reports – Drs. Plunkett, Singh and Zelikoff – disregarded its findings without offering a legitimate basis to do so.[62] Plaintiff assert that Wehner does not, as a factual matter, undermine their experts' migration theory. This is false. As explained in the J&J defendants' opening brief, Wehner involved the repeated, direct deposit of ***cosmetic talc*** into the posterior fornix of the vaginas (i.e., near the cervix) of cynomolgus monkeys

59 (*Id*.)

60 (Pls.' Opp'n at 42-43 (citing Wehner 1986).)

61 (*Compare id*. at 42 n.120 (pointing to the reports of Drs. Plunkett, Singh and Zelikoff as evidence that plaintiffs' experts considered Wehner) *with* Defs.' Br. at 36 n.68 (stating that only Plunkett, Singh and Zelikoff addressed Wehner in their reports).)

62 (*See* Defs.' Br. at 37-38.)

who were treated with oxytocin and restrained with their pelvises raised – yet observed ***no migration of talc to the oviducts***.[63] Thus, the study directly contradicts plaintiffs' experts' unsubstantiated theory that talc dusted externally on the perineum migrates to the ovaries. And while plaintiffs argue that Wehner is irrelevant because it "predates" Sjösten (2004) and Kunz (1997), those human studies also do not support the theory that talc dusted externally on the perineum migrates to the ovaries and fallopian tubes because they involved the forced application of substances other than talc directly into the body, as explained in detail above. Moreover, plaintiffs' argument misses the point, which is that plaintiffs' experts' reliance on cherry-picked animal studies involving rodents is inherently unreliable because they largely ignore or dismiss the most factually analogous animal study. *See In re Zoloft (Sertraline Hydrochloride) Prods. Liab. Litig.*, 26 F. Supp. 3d 449, 465 (E.D. Pa. 2014) (excluding expert who "failed to acknowledge and distinguish or otherwise address the research findings contrary to her litigation opinion").

B. Plaintiffs' Experts Lack Reliable Evidence That Perineally-Applied Talc Can Reach The Fallopian Tubes Or Ovaries Through Inhalation Or Lymphatic Transport.

Plaintiffs' experts' alternative theory as to how cosmetic talc purportedly reaches the ovaries and fallopian tubes – inhalation and transport through the

63 (*Id.* at 36-38.)

lymphatic system – is equally unsupported by the scientific evidence they cite. As explained in the J&J defendants' opening brief, the International Agency for Research on Cancer ("IARC") has expressly concluded that there is "insufficient evidence of carcinogenicity [of talc to the ovaries] by the inhalation route," and even plaintiffs' own experts have acknowledged that no published articles demonstrate that talc can be inhaled and then transported to the ovaries.[64] Further, plaintiffs' experts' inhalation theory is inherently implausible because it is based on a presumption that talc travels through the lymphatic system and organs causing inflammation that leads to cancer, yet there is zero evidence that talc exposure is associated with other cancers in the lymph nodes or other organs more proximate to the respiratory system.[65] Plaintiffs' responses to these arguments fall decidedly flat.

First, plaintiffs attempt to skirt the fact that there are no studies supporting the hypothesis that inhaled talc migrates to the ovaries through the lymphatic

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64 (*See* Defs.' Br. at 41-42 (citing, *e.g.*, Carson Rep. at 4 (conceding that IARC "concluded that there [was] 'insufficient evidence of carcinogenicity by the inhalation route'"); Dep. of Patricia G. Moorman, M.S.P.H., Ph.D. 303:17-304:14, Jan. 25, 2019 (attached as Ex. B39 to Tersigni Cert.) (acknowledging that "epidemiologic studies have not specifically addressed the risk associated with inhalation only of talcum powder products"); Singh Dep. 216:14-19 (agreeing with statement that "studies of talcum powder use failed to show a statistically significant association between nongenital use of talcum powder and ovarian cancer")).)

65 (*See id*. at 47.)

system by referring to it as merely a "possible" or "secondary mechanism."[66] The J&J defendants agree that for the most part, plaintiffs' experts barely address inhalation in their reports and do not even attempt to point to any evidence that it is a viable route of exposure. But this is a reason to exclude such opinions, not a basis for excusing plaintiffs of their burden to establish that their experts' theories on biological plausibility are supported by reliable scientific evidence.

Second, plaintiffs assert that it does not matter that their experts lack evidence that inhaled talc is able to travel through the lymphatic system to the ovaries because they allege that the cosmetic talc products at issue "contain asbestos and fibrous talc, which have been shown to migrate when inhaled."[67] But, as explained in the J&J defendants' briefing with respect to plaintiffs' experts' asbestos opinions, there is no reliable scientific evidence that the products contain asbestos at all.[68] And even if there were, neither plaintiffs nor their experts can point to any evidence demonstrating that there is a mechanism by which asbestos migrates to the ovaries. Instead, plaintiffs rely almost entirely on a 2012 IARC

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66 (Pls.' Opp'n at 43, 46.)

67 (*Id.* at 44.)

68 (*See generally* Defs.' Mem. of Law in Supp. of Mot. to Exclude Pls.' Experts' Asbestos-Related Ops. ("Defs.' Asbestos *Daubert* Br."), May 7, 2019 (ECF No. 9736-3).) Plaintiffs' experts also lack reliable support for their opinions that fibrous talc is carcinogenic, as explained in detail in the J&J defendants' briefing in support of their Motion To Exclude Plaintiffs' Experts' Opinions Regarding Alleged Heavy Metals and Fragrances In Johnson's Baby Powder And Shower To Shower. (*See* ECF No. 9736-4.)

monograph, which notes an association in the ***epidemiological literature*** between ovarian cancer and ***significant occupational exposure to asbestos***.[69] But epidemiological findings cannot serve as evidence of a biologically plausible ***mechanism*** by which particulates can move through the body. Moreover, the type and amount of exposure in those studies renders them entirely inapposite. Here, even plaintiffs' own experts only purport to have identified a miniscule amount of asbestos in samples of the Products, in the range of 3.3 millionths of a percent.[70] As explained by Dr. Nadia Moore, the only expert in this litigation who has analyzed the amount of asbestos exposure that would result if plaintiffs' experts' findings were reliable, the cumulative lifetime exposure to the level of asbestos plaintiffs claim is present in cosmetic talc is at least 4,000 times below the Occupational Safety and Health Administration's ("OSHA") permissible lifetime exposure limit.[71]

Third, plaintiffs contend that their experts' "secondary" inhalation theory is sufficiently supported, but all they point to are irrelevant studies that have nothing to do with whether talc can travel through the lymphatic system to the ovaries. For example, plaintiffs argue that Dr. Zelikoff, one of the few experts who offers any

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69 (Pls.' Opp'n at 44 (citing Int'l Agency for Research on Cancer, World Health Org., 100 *Monographs on the Evaluation of Carcinogenic Risks to Humans: Arsenic, Metals, Fibres, and Dusts* 219, 232, 256, 280 (2012)).)

70 (Defs.' Asbestos *Daubert* Br. at 3.)

71 (*Id*. at 85.)

analysis on the issue of inhalation, reliably premises her opinions on studies observing substances (not always talc) in the lung and other, ***non-reproductive*** tissue of animals that were directly injected with such substances, asserting that these studies support the general "scientific premise for the movement of particles of a certain size throughout the body."[72] But establishing that particles move around after they are directly inserted into the body of a rat or other animal comes nowhere close to making it biologically plausible that cosmetic talc can be inhaled, travel through the entire human body and lodge itself in the ovaries or fallopian tubes specifically.[73] Similarly, while plaintiffs assert that pathology findings of talc in ovarian and lymph node tissue by Heller and Cramer, respectively, support their experts' inhalation theories,[74] they have nothing but speculation to connect these findings to inhaled talc. Indeed, these are the very same studies that plaintiffs' experts point to as evidence that talc migrates up the genital tract from the perineum. But the fact is that no one – not Heller, Cramer or plaintiffs' experts – has any basis to determine where the talc purportedly identified in that tissue originated.

Fourth, plaintiffs cannot refute that any theory that inhaled talc moves throughout the entire body via the lymphatic system, resulting in chronic

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72 (*See* Pls.' Opp'n at 45-46.)

73 (*See* Defs.' Br. at 41-45.)

74 (*See* Pls.' Opp'n at 45-46.)

inflammation that causes cancer, is inherently implausible given that there is no evidence that talc exposure causes inflammation and/or cancer in the lymph nodes or any other organ that it would also reach through this alleged mechanism.[75] Indeed, plaintiffs' only real response is to assert that "different tissues react differently to carcinogens" and therefore some tissues may be "more susceptible to a carcinogen than others."[76] But, as discussed in more detail below, this position directly undermines their experts' reliance on studies involving cancers of organs and tissue ***other than the ovaries*** as evidence that chronic inflammation is capable of causing ovarian cancer. Simply put, plaintiffs cannot have it both ways: if their experts take the position that talc and its constituent components cause inflammation all over the body that can progress to cancer, then they must explain why there is no evidence of cancer in other organs purportedly exposed to talc.

For all of these reasons, plaintiffs cannot refute that their experts lack scientific support for their hypothesis that cosmetic talc dusted externally on the perineum is capable of reaching the ovaries – and therefore even the first link in the chain of these experts' tenuous biological plausibility opinions fails.

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75 (*See* Defs.' Br. at 45-46.)

76 (Pls.' Opp'n at 46.)

IV. PLAINTIFFS' EXPERTS HAVE NO EVIDENCE OF A PLAUSIBLE MECHANISM BY WHICH TALC COULD CAUSE OVARIAN CANCER EVEN IF IT REACHED THE FALLOPIAN TUBES OR OVARIES.

Plaintiffs also cannot refute that their experts lack relevant scientific support for the other necessary piece of their biological plausibility theory: a mechanism by which talc can cause cancer even if it does get to the ovary or fallopian tubes. Plaintiffs' experts advance two alternative causation hypotheses: (1) that talc results in chronic inflammation capable of causing the various subtypes of ovarian cancer; or (2) that talc increases the risk of all ovarian cancers by inhibiting MUC1 antibodies. But plaintiffs' experts lack any scientific evidence that either theory is biologically plausible.[77]

A. The Evidence Plaintiffs Cite Does Not Demonstrate That It Is Biologically Plausible That Talc Causes Chronic Inflammation In The Genitourinary Tract Or That Chronic Inflammation Causes Ovarian Cancer.

1. There Is No Evidence That Talc Causes Chronic Inflammation In The Genitourinary Tract.

As the J&J defendants explained in their opening brief, the studies cited by plaintiffs' experts for the proposition that talc causes the type of chronic

[77] Fourteen of plaintiffs' experts opine that talc causes chronic inflammation in ovarian tissue, which allegedly leads to ovarian cancer. (*See, e.g.*, Saed Rep. at 20; Zelikoff Rep. at 26; Kane Rep. at 4; Moorman Rep. at 39-40; Expert Report of Shawn Levy, Ph.D. at 11-13, Nov. 16, 2018 (attached as Ex. C39 to Tersigni Cert.); Carson Rep. at 7; Clarke-Pearson Rep. at 4, 9-10; McTiernan Rep. at 62-63; Plunkett Rep. at 46-47; Siemiatycki Rep. at 64-66; Singh Rep. at 58-59, 65; Smith-Bindman Rep. at 12-13; Smith Rep. at 17-18; Wolf Rep. at 11-13.)

inflammation that they claim is capable of causing cancer do not support that point and, in fact, the small body of relevant research indicates that talc identified in human tissue does ***not*** initiate such an inflammatory response.[78] All of plaintiffs' arguments in response misconstrue the science and misrepresent plaintiffs' burden to establish that their experts' opinions are based on a reliable methodology.

First, plaintiffs argue that the fact that the studies relied on by their experts for the proposition that talc has been identified in human ovarian tissue found ***no evidence*** of inflammation in that tissue[79] "has nothing to do with *Daubert*" because "[w]hether [p]laintiffs are correct" on this point is a matter for the jury.[80] But the issue here is not the correctness of plaintiffs experts' ultimate conclusions; it is whether whose conclusions are based on a reliable methodology. As set forth in detail in the J&J defendants' various motions to exclude plaintiffs' experts' testimony, the law is clear that opinions are ***not*** based on a sound methodology where they are not supported by the sources upon which the experts rely or fail to take into account the totality of the relevant scientific evidence. *See, e.g.*, *Heller v. Shaw Indus., Inc.*, 167 F.3d 146, 159 (3d Cir. 1999) (expert's testimony on causal

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78 (*See* Defs.' Br. at 50-54.)

79 (*See id*. at 50 (citing Heller et al., *The Relationship Between Perineal Cosmetic Talc Usage and Ovarian Talc Particle Burden*, 174 Am. J. Obstet. Gynecol. 1507 (1996) ("Heller (1996) – Talc") (attached as Ex. A60 to Tersigni Cert.); Henderson et al., *Talc and Carcinoma of the Ovary and Cervix*, 78 J Obstet Gynaecol Br Commonw. 266 (1971)).)

80 (Pls.' Opp'n at 48.)

relationship between carpet installation and plaintiff's illness was properly excluded because such a conclusion "did not reliably flow from th[e] data and methodology"); *Schepise v. Saturn Corp.*, No. CIV.A. 94-385(MLP), 1997 WL 897676, at *16-17 (D.N.J. July 30, 1997) (Wolfson, J.) (excluding expert who relied on studies that did not support her conclusions).

That is precisely the case here. Plaintiffs' experts have taken the position that talc finds its way to ovarian tissue, citing pathology studies, but then essentially ignore the fact that those same studies found no evidence of ***any*** inflammation – much less the type of chronic inflammation that the experts claim can cause cancer – in that tissue. This is especially problematic because, as set forth in the J&J defendants' opening brief, plaintiffs are unable to point to any other reliable evidence that talc ***does*** cause chronic inflammation in ovarian tissue.[81] Further, plaintiffs' assertion that inflammation may have been present in

[81] In the fact section of their opposition brief, plaintiffs cite a variety of studies that they assert "have concluded that talcum powder causes an inflammatory response." (Pls.' Opp'n at 21-23.) But plaintiffs do not even bother to reference such studies in the argument section of their brief, likely because they do not actually support this proposition. For example, plaintiffs rely primarily on epidemiological studies, which – by their very nature – cannot serve as scientific evidence that there is a ***biological mechanism*** by which talc causes inflammation. This is especially true given that, at bottom, the epidemiological studies do nothing more than note the hypothesis that talc could cause inflammation. *See, e.g.*, Penninkilampi & Eslick, *Perineal Talc Use and Ovarian Cancer: A Systematic Review and Meta-Analysis*, 29 Epidemiol. 41, 45 (2018) (attached as Ex. A109 to Tersigni Cert.) (noting that "the evidence remains insufficient to understand the mechanism with any reasonable certainty"). The *in vivo* and *in vitro* studies cited

the tissue examined in these studies but simply was not "seen" or was "consumed by the cancer over time"[82] is pure speculation. Indeed, the only support plaintiffs cite for the proposition that existing, chronic inflammation "is not necessarily seen" in pathology (beyond their own experts' say-so), is Hanahan (2011), which states the opposite. According to that study, while "in the course of normal wound healing and fighting infections, immune inflammatory cells appear transiently and then disappear," this is "***in contrast to their persistence in sites of chronic inflammation***" where they appear in pathology.[83] Thus, plaintiffs' experts' dismissal of findings that inflammation does ***not*** occur around talc observed in ovarian tissue renders their opinions inherently unreliable.

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by plaintiffs are similarly unhelpful because they do not address the issue of whether talc can cause chronic inflammation in the ovarian or fallopian tubes, but instead evaluate potential effects of talc (or, in some cases, different particles) on lung or other non-reproductive tissue. *See, e.g.*, Kahn et al., *Nano-talc Stabilized TNF-m-RNA I Human Macrophages*, 7 J. Biomed. Nanotech. 112, 113 (2011) (attached as Ex. 90 to Pls.' Opp'n); Akhtar et al., *Cytotoxicity and Apoptosis Induction by Nanoscale Talc Particles from Two Different Geographical Regions in Human Lung Epithelial Cells*, 29 Envtl. Toxicol. 394, 404 (2012) ("Akhtar 2012") (attached as Ex. 92 to Pls.' Opp'n). None of these sources supports the hypothesis that talc causes chronic inflammation that could lead to ovarian cancer, and plaintiffs' attempt to suggest otherwise only highlights how far they and their experts have strayed from reliable scientific methodology.

82 (Pls.' Opp'n at 48.)

83 Hanahan & Weinberg, *Hallmarks of Cancer: The Next Generation*, 144 Cell 646, 664 (2011) ("Hanahan 2011") (attached to Pls.' Opp'n as Ex. 75) (emphasis added).

Second, plaintiffs attempt to defend their experts' reliance on Keskin (2009) – in which researchers observed infection and acute granulomas in rats sprayed with aerosolized talc but no chronic inflammation or neoplastic changes – by speculating that chronic inflammation ***might*** have been seen by Keskin if the study period had been longer.[84] But this is nothing more than rank speculation.[85]

Third, plaintiffs also resort to speculation in addressing their experts' failure to explain why talc would cause inflammation in the ovaries but not in other intermediate tissues – such as the vagina, fallopian tube, cervix and endometrium – that likewise would be exposed to talc under their migration theory.[86] According to plaintiffs, "these different areas (e.g., vagina) have different tissues" and therefore might react differently to potential carcinogens, especially if talc particles lodge in ovarian tissue, but not cervical or endometrial tissue.[87] But neither

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84 (Pls.' Opp'n at 49-50.)

85 Plaintiffs also assert that J&J's critique of Dr. Saed is "unavailing" because he "mistakenly cited Langseth (2004) instead of Langseth (2008)." (Pls.' Opp'n at 50.) Defendants, of course, had no way of knowing that Dr. Saed cited the wrong article in his report. In any event, Langseth (2008) does not help plaintiffs either. The only mention of inflammation in that article – which does not provide any new data but just summarizes other studies – indicates that ovarian carcinogenicity "***may be related*** to inflammation." Langseth 2008 at 359 (emphasis added). The authors conclude that "[t]he current body of experimental and epidemiological evidence is ***insufficient to establish a causal association between perineal use of talc and ovarian cancer risk***" and that "[e]xperimental research is needed . . . to evaluate the ovarian carcinogenicity of talc." *Id.* (emphasis added).

86 (*See* Defs.' Br. at 54 n.122.)

87 (Pls.' Opp'n at 50-51.)

plaintiffs nor their experts have valid scientific support for these assertions. Further, as set forth below, plaintiffs' position that different tissues react differently to alleged carcinogens merely underscores how inappropriate it is for their experts to rely on literature regarding the purported connection between chronic inflammation and ***cancers of organs and tissue outside the reproductive system*** to opine that ovarian cancer, specifically, is caused by inflammation.

In sum, plaintiffs' experts are unable to point to any reliable, scientific support for the theory that talc causes chronic inflammation, and the literature they do cite does not, in fact, support that hypothesis. For this reason, too, their experts' opinions regarding biological plausibility are inadmissible.

2. Plaintiffs' Experts' Opinions Are Also Unreliable Because They Cannot Point To Scientific Studies Supporting The Theory That Chronic Inflammation Causes Ovarian Cancer.

Plaintiffs' biological plausibility theory is also unreliable for another, independent reason: plaintiffs' experts offer no evidence to support their conclusion that chronic inflammation can cause any particular subtype of ovarian cancer.[88] In response, plaintiffs: (1) attempt to shore up their experts' opinions with studies purportedly establishing a link between chronic inflammation and epithelial ovarian cancer; (2) insist that NSAID studies provide evidence of the role of inflammation in cancer pathogenesis "generally"; and (3) maintain that PID

[88] (Defs.' Br. at 54-66.)

is associated with an increased risk of high grade serous carcinoma. As set forth below, these arguments lack merit.

First, plaintiffs argue that researchers have "concluded that inflammation plays a critical role in the pathogenesis of epithelial ovarian cancer."[89] But none of the articles that plaintiffs cite lends any reliable support to that assertion.

For example, while plaintiffs rely heavily on Ness (1999), Shan (2009) and Savant (2018), these are all review articles that do not contain any original data or findings related to causation or biological plausibility. This alone renders them unhelpful in determining whether plaintiffs' novel theory has any reliable support. *See Mallozzi v. EcoSMART Techs., Inc.*, No. 11-CV-2884 (SJF) (ARL), 2013 WL 2415677, at *5, *7 (E.D.N.Y. May 31, 2013) (excluding plaintiffs' expert's general causation opinion where the expert "has not justified his reliance" on the conclusion of a review article because he "provided no analysis of, and apparently did not review, the clinical trials that were reviewed in the article"); *cf. Mitchell v. Sec'y of Health & Human Servs.*, No. 13-948V, 2017 WL 3816078, at *8 (Fed. Cl. Aug. 7, 2017) (concluding that the petitioner's expert had not presented sufficient evidence to establish that the vaccination had caused his injuries and noting that one of the studies was a "review article that contains no original data or research" to support his claim). Moreover, while some of these articles suggest that

[89] (Pls.' Opp'n at 52.)

inflammation is associated with the development of epithelial ovarian cancer, plaintiffs do not cite any studies supporting that proposition[90] and rely on outdated theories that have been discredited in recent years.[91] Indeed, Dr. Mossman

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[90] For example, plaintiffs cite Ness (1999) as stating that "inflammation initiators . . . play a role in ovarian carcinogenesis" (Pls.' Opp'n at 52 (citing Ness & Cottreau, *Possible Role of Ovarian Epithelial Inflammation in Ovarian Cancer*, 91 J. Nat'l Cancer Inst. 1459, 1464 (1999) ("Ness 1999") (attached as Ex. A105 to Tersigni Cert.))) but, as explained in the J&J defendants' opening brief, Ness expressly notes that "observational and experimental data will be needed to confirm the hypothesis that inflammation is a central biologic process in ovarian cancer risk," Ness 1999 at 1459. In addition, plaintiffs quote a statement in Shan (2009) that "[i]ncreasing evidence suggests that inflammation contributes significantly to the etiology of [epithelial ovarian cancer]." (Pls.' Opp'n at 26 n.73 (quoting Shan 2009 at 3110).) But Shan does not point to any scientific studies or other data supporting that statement. Plaintiffs also point to a statement in Savant (2018) that "[u]nresolved, chronic inflammation is a critical risk factor for tumor initiation." (Pls.' Opp'n at 26 n.73 (quoting Savant 2018 at Figure 1).) This statement accompanies a figure that purports to illustrate sources of inflammation in the ovary, and it, too, is unsupported by any studies. Moreover, even when these review articles do cite to primary data, those data often do not support the point being made by the articles' authors. The Savant article, for instance, asserts that exposure to talc "can cause inflammation of the ovaries and poses a risk hazard for the development of [epithelial ovarian cancer]." Savant 2018 at 5. But the only support provided for this statement is Heller (1996) – Talc, which examined the relationship between perineal talc usage and ovarian talc particle burden. And Heller (1996) – Talc – which identified talc particles in both users and non-users – ***did not find chronic inflammation in the ovaries***. *See* Heller (1996) – Talc (noting that although talc was detected in the ovaries, "[t]here was no evidence of response to talc, such as foreign body giant cell reactions or fibrosis in the tissue").

[91] Both Shan and Savant suggest that tubal ligation reduces the risk of ovarian cancer because it prevents inflammation caused by the introduction of foreign material through the vagina. *See* Savant 2018 at 5 ("Tubal ligation, which is protective for EOC, is thought to block the transport of talc from the lower genital tract," preventing it from "triggering an inflammatory response."); Shan 2009 at 3108 ("[H]ysterectomy and tubal ligation, both of which cut off the passage of

described the Savant article as "a very sloppy paper with inconsistent statements that are not supported by the references" it cites.[92]

Plaintiffs' attempts to defend their experts' reliance on Trabert (2014) and Buz'Zard (2007)[93] are also unpersuasive. As explained in the J&J defendants' opening brief, Trabert (2014) investigated 46 inflammatory serum markers for possible association with ovarian cancer, finding that only two were associated with a risk of developing ovarian cancer.[94] As plaintiffs are forced to acknowledge,

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inflammatory factors from the lower to the upper genital tract, afford[] protection against EOC."). But, as a number of recent studies have shown, tubal ligation is associated with "a reduced presence and decreased proliferation of progenitor cells" and "compositional and functional changes." (Kurman Rep. at 23-24 (quoting Tiourin et al., *Tubal Ligation Induces Quiescence in the Epithelia of the Fallopian Tube Fimbria*, 22 Reproductive Scis. 1262 (2015) ("Tiourin 2015")).) It is now understood that these changes – and not any protection from the purported effects of migration of environmental carcinogens – explain why tubal ligation reduces the risk of high grade serous carcinoma. (*See id.*; *see also* Shih Rep. at 16 (citing Roy et al., *Fimbrio-Ovarian Relationship in Unexplained Infertility*, 60 Gynec. Obstet. Invest. 128 (2005) and Huang et al., *Mutagenic, Surviving and Tumorigenic Effects of Follicular Fluid in the Context of p53 Loss: Initiation of Fimbria Carcinogenesis*, 36 Carcinogenesis 1419 (2015)) (explaining that alteration of the tubal fimbriated ends is now thought to reduce "the carcinogenic events of fallopian tube epithelium and prevent[] the occurrence of ovarian cancer precursor lesions on the fallopian tubes"); Birrer Rep. at 10 (citing Tiourin 2015) (noting that "recent data have demonstrated that there are dramatic effects on the cells at the distal end of the fallopian tube cells after a tubal ligation").)

92 (Mossman Dep 291:23-292:2.)

93 (Pls.' Opp'n at 53-54.)

94 (Defs.' Br. at 57-58 (citing Trabert et al., *Pre-Diagnostic Serum levels of Inflammation Markers and Risk of Ovarian Cancer in the Prostate, Lung,*

"the results of Trabert's study were inconclusive"[95] – and this concession alone renders the study an insufficient foundation for showing that plaintiffs' proposed biological mechanism is more than theoretically possible. *See Henricksen*, 605 F. Supp. 2d at 1176 (rejecting expert causation opinions for lack of biological plausibility where the relevant studies "make clear that the connection" between the substance and disease at issue "is at this point in time only a hypothesis in need of further investigation"). This is especially true given that Trabert studied serum markers associated with systemic inflammation throughout the body – not chronic inflammation specific to the ovaries, which is what plaintiffs' experts hypothesize is caused by talc. With respect to Buz'Zard (2007) – in which the authors purportedly observed the effects of talc on various types of human cells[96] – plaintiffs claim that defendants "provide[] no explanation for why the use of immortalized cells eliminates the[] results" of that study.[97] Not so; as the J&J defendants explained in their opening brief, use of immortalized cells instead of

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Colorectal and Ovarian Cancer (PLCO) Screening Trial, 135 Gynecol. Oncol. 297 (2014) ("Trabert 2014 – Serum") (attached as Ex. A143 to Tersigni Cert.)).)

95 (*Id.* at 53.)

96 (*See* Defs.' Br. at 58-59 (citing Buz'Zard & Lau, *Pycnogenol® Reduces Talc-induced Neoplastic Transformation in Human Ovarian Cell Cultures*, 21 Phytother. Res. 579 (2007) (attached as Ex. A16 to Tersigni Cert.)).)

97 (Pls.' Opp'n at 54.)

normal ovarian cells "could affect the reaction observed."[98] For example, the antigen used to immortalize ovarian surface epithelial cells "is a viral gene product that evokes changes equivalent to at least two of the transformation events needed for ovarian carcinogenesis" and renders the cells "genetically unstable."[99] Both of these considerations render this immortalized cell line particularly "inapt for studying the mechanisms of ovarian carcinogenesis."[100] Moreover, plaintiffs ignore the host of other methodological problems with the Buz'Zard study outlined in defendants' opening brief and in defendants' experts' reports.[101] For all of these reasons, plaintiffs' continued reliance on Buz'Zard is misplaced.

Plaintiffs also cite a number of other publications in the background section of their brief that they claim demonstrate that "the link between chronic inflammation and ovarian cancer is well-supported."[102] They do not, however, address any of these sources in their argument, perhaps because a significant number of them ***were not cited*** in their experts' reports and therefore could not

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98 (Defs.' Br. at 59 & n.137 (citing Birrer Rep. at 14; Neel Rep. at 25; Kurman Rep. at 18).)

99 (Neel Rep. at 25.)

100 (*Id.*)

101 (Defs.' Br. at 59-60 (citing Birrer Rep. at 14-15; Neel Rep. at 25-26; Kurman Rep. at 18).)

102 (Pls.' Opp'n at 23.)

possibly provide a reliable basis for those experts' opinions.[103] *See In re Breast Implant Litig.*, 11 F. Supp. 2d 1217, 1231 (D. Colo. 1998) (finding that additional articles and studies submitted by plaintiffs "cannot properly be considered as additional support for [expert] witnesses' methodology or conclusions" because "[n]one of the [p]laintiffs' expert witness reports referred to any of these additional studies or articles"); *Rondigo, L.L.C. v. Casco Twp., Mich.*, 537 F. Supp. 2d 891, 896-97 (E.D. Mich. 2008) (concluding that plaintiffs could not defend their expert's opinions by pointing to materials "the report *does not* rely on"); *see also, e.g.*, *Tamraz v. Lincoln Elec. Co.*, 620 F.3d 665, 672 (6th Cir. 2010) (rejecting counsel's effort to redefine a proposed expert's opinion in response to a *Daubert* challenge); *In re Human Tissue Prods. Liab. Litig.*, 582 F. Supp. 2d 644, 667 (D.N.J. 2008) (if expert fails to adequately support his or her opinion, "counsel

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[103] (*See, e.g.*, Nat'l Acads. of Scis., Eng'g & Med., *Ovarian Cancers: Evolving Paradigms in Research and Care*, Nat'l Acads. Press (2016) ("NASEM 2016") (attached as Ex. 70 to Pls.' Opp'n) (cited in Pls.' Opp'n at 24 n.65); Hanahan 2011 at 659 (cited in Pls.' Opp'n at 25 n.72, 48 n.42); Yan et al., *Molecular Analysis of Genetic Instability Caused by Chronic Inflammation*, 512 Cancer 15 (2009) (attached as Ex. 74 to Pls.' Opp'n) (cited in Pls.' Opp'n at 25 n.72); Belotte et al. 2014, *The Role of Oxidative Stress in the Development of Cisplatin Resistance in Epithelial Ovarian Cancer*, 21 Reproductive Scis. 503 (2014) (attached as Ex. 86 to Pls.' Opp'n) (cited in Pls.' Opp'n at 28 n.76); Peres et al., *Analgesic medication use and risk of epithelial ovarian cancer in African American women*, 114 Br J Cancer 819 (2016) ("Peres 2016") (attached as Ex. 108 to Pls.' Opp'n) (cited in Pls.' Opp'n at 57 n.174); Stewart et al., *Risk of High-Grade Serous Ovarian Cancer Associated with Pelvic Inflammatory Disease, Parity and Breast Cancer*, 55 Cancer Epidemiol. 110 (2018) ("Stewart 2018") (attached as Ex. 110 to Pls.' Opp'n) (cited in Pls.' Opp'n at 59); Akhtar 2012 (cited in Pls.' Opp'n at 30 nn.81 and 84).)

cannot fill in the gaps"); *In re Rezulin*, 369 F. Supp. 2d at 407 ("The subject of this motion is the proposed testimony of experts, not the theories of the lawyers.").

Moreover, these articles – which address systemic inflammation throughout the body – do not reliably support plaintiffs' theory that localized inflammation in reproductive tissue causes ovarian cancer. To the contrary, some of the articles directly contradict plaintiffs' experts' assumptions that chronic inflammation causes ovarian cancer. Most notably, Liou (2010), Reuter (2010) and Crusz (2015)[104] suggest that ***ovarian cancer causes inflammation*** – not the other way around – a point that defendants' experts also make.[105] Liou (2010), for example, examines cell signaling pathways present in ***ovarian cancer cells***.[106] Likewise, Reuter (2010) discusses generalized inflammation and ovarian cancer in the context of chemoresistance and cancer stem cell survival – both of which are only

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104 (*See* Pls.' Opp'n at 23-24 nn.65, 67.)

105 (*See, e.g.*, Shih Rep. at 15 ("chronic inflammation observed in ovarian cancer is most likely a result of cancer, not the cause").)

106 *See* Liou & Storz, *Reactive Oxygen Species in Cancer*, 44 Free Radic. Res. 479, 482 (2010) (attached as Ex. 64 to Pls.' Opp'n) ("It was recently shown that increased [extracellular-regulated kinase 1/2] activity ***in ovarian cancer cells*** . . . results from sustained ubiquitination and loss of endogenous [mitogen-activated protein kinase phosphatase 3] . . . .") (emphasis added) (footnote omitted); *id.* at 483 ("Hydrogen peroxide generated by epithelial growth factor . . . ***in human ovarian cancer cells*** activates Akt and p70 S6K1, a substrate of Akt that regulates protein synthesis.") (emphasis added) (footnote omitted).

implicated once cancer is already present.[107] And Crusz (2015) mentions ovarian cancer in the authors' discussion of "[a]nti-inflammatory agents tested in clinical trials in ***patients with cancer***."[108] In addition, a number of the articles cited by plaintiffs do not even address epithelial ovarian cancer (much less any of its subtypes).[109] And the remainder of the articles treat plaintiffs' inflammation theory as just that – a hypothesis in need of further investigation before any conclusions can be drawn.[110] In short, none of the scientific literature provides any

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[107] Reuter et al., *Oxidative Stress, Inflammation, and Cancer: How Are They Linked?*, 49 Free Radic. Biol. Med. 1603, 1609-10 (2010) (attached as Ex. A110 to Tersigni Cert.).

[108] Crusz & Balkwill, *Inflammation and Cancer: Advances and New Agents*, 12 Nature 584, 587-80, 591, 593 (2015) (attached as Ex. 66 to Pls.' Opp'n).

[109] *See* Okada, *Beyond Foreign-Body Induced Carcinogenesis: Impact of Reactive Oxygen Species Derived From Inflammatory Cells in Tumorigenic Conversion and Tumor Progressions*, 121 Int J Cancer 2364 (2007) (cited in Pls.' Opp'n at 23 n.65) (discussing tumor development generally); Grivennikov et al., *Immunity, Inflammation, and Cancer*, 140 Cell 883 (2010) (attached as Ex. 65 to Pls.' Opp'n) (cited in Pls.' Opp'n at 23-24 n.65) (discussing tumorigenesis generally and further positing that "not all chronic inflammatory diseases increase cancer risk and some of them, such as psoriasis, may even reduce it") (cited in Pls.' Opp'n at 23-24 n.65); Kiraly et al., *Inflammation, DNA Damage and Mutations In Vivo*, 11 PLO Genetics 1 (2015) (attached as Ex. 68 to Pls.' Opp'n) (cited in Pls.' Opp'n at 24 n.65) (studying pancreatic inflammation). Notably, plaintiffs' reliance on studies that have nothing to do with ovarian cancer seriously undermines their contention elsewhere that "different tissues react differently to carcinogens." (Pls.' Opp'n at 46.)

[110] *See* Balkwill 2001 at 539 (abstract) (cited in Pls.' Opp'n at 23 n.65) (stating that "cancer susceptibility and severity ***may be*** associated with functional polymorphisms of inflammatory cytokine genes" and calling for "***further investigation*** of non-steroidal anti-inflammatory drugs in the chemoprevention and treatment of malignant diseases") (emphases added); Coussens & Werb,

evidence to support the notion that chronic inflammation is a plausible mechanism for the development of ovarian cancer.

Second, plaintiffs insist that NSAID studies provide "additional evidence of the role of inflammation in cancer pathogenesis generally."[111] But, as explained in defendants' opening brief – and as plaintiffs' experts concede – the studies

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Inflammation and Cancer, 420 Nature 860 (2002) (attached as Ex. 62 to Pls.' Opp'n) (cited in Pls.' Opp'n at 23 n.65) (one "***hypothesis*** is that many malignancies arise from areas of infection and inflammation") (emphasis added); Trabert 2014 – Serum (cited in Pls.' Opp'n at 24 n.65) (noting that "the implications of the findings" of the study were "unclear and do not substantiate a link between local inflammation and ovarian cancer"); NASEM 2016 at 110 (cited in Pls.' Opp'n at 24 n.65) (stating that some studies "***suggest*** a ***possible association*** between inflammation and an increased risk of ovarian cancer"); Ness 1999 at 1463 (cited in Pls.' Opp'n at 26 n.73) ("Further observational and experimental data will be needed to confirm the hypothesis that inflammation is a central biologic process in ovarian cancer risk."); Saed et al., *New Insights into the Pathogenesis of Ovarian Cancer: Oxidative Stress*, in *Ovarian Cancer – From Pathogenesis to Treatment* (2018) (cited in Pls.' Opp'n at 26 n.73) (concluding that the "precise mechanism" explaining the association between talc use and ovarian cancer has "yet to be elucidated"); Health Canada, Draft Screening Assessment: Talc ($Mg_3H_2(SiO_3)_4$) (Chem. Abstracts Serv. Registry No. 14807-96-6) (2018) (attached as Ex. A58 to Tersigni Cert.) (stating that the "etiology of most ovarian tumours, in general, has not been well established" and that the "specific mechanism(s) and cascade of molecular events by which talc might cause ovarian cancer have not been identified"). Moreover, as a number of defendants' experts explained, many of these studies fail to "distinguish between whether the inflammation [observed] is a marker of ***existing*** ovarian cancer or . . . a ***cause*** of cancer." (Neel Dep. 296:23-297:8 (emphasis added) (discussing the National Academies of Science chapter); *see also id.* 111:21-112:20 (discussing the Hanahan article and explaining that "you have to distinguish between inflammation that accompanies cancer and those cancers that have a component of inflammation in their initiation").)

[111] (Pls.' Opp'n at 55.)

examining the effect of anti-inflammatory drugs on ovarian cancer risk are "inconsistent" at best.[112] Apparently recognizing that their experts' opinions regarding NSAIDs stand on shaky ground, plaintiffs offer the disclaimer that NSAID data is not the whole basis for their experts' opinions regarding inflammation[113] and maintain that their experts acknowledged that the data on the link between NSAID use and inflammation is "mixed."[114] But these arguments miss the point. With the exception of Dr. Kane, plaintiffs' experts failed to even mention (much less discuss) one of the largest and most inclusive meta-analyses of the relevant NSAID studies, Baandrap (2013), which definitively concluded that there is no statistically significant association between NSAID use and the prevention of ovarian cancer.[115] And although Dr. Kane nominally cited Baandrap (2013), she did not in any way address its findings undermining a protective role for NSAIDs.[116] In other words, plaintiffs' experts' conclusions that NSAID use decreases ovarian cancer risk are directly contradicted by evidence that they completely ignored. This, too, undermines the reliability of their opinions. *See Zoloft*, 26 F. Supp. 3d at 461.

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112 (Defs.' Br. at 64-66 (quoting Smith Rep. at 18).)

113 (Pls.' Opp'n at 54-55.)

114 (*Id.* at 55.)

115 (*See* Defs.' Br. at 64-66.)

116 (*See id.* at 65 n.162.)

Moreover, plaintiffs' selective citation to studies is misleading and should be rejected. For example, plaintiffs cite Trabert (2014), for the proposition that there was a 34% decrease in ovarian cancer risk associated with regular use of low-dose aspirin,[117] but they fail to mention that the study only found a reduction of risk associated with use of aspirin, not other NSAIDs.[118] Plaintiffs also rely on Trabert (2019), but fail to explain that the decrease in ovarian cancer risk identified there was only 10%, that it was only observed in individuals who used aspirin for less than 10 years, and that there was either ***no risk or an increased risk*** associated with both the use of other NSAIDs and the use of aspirin for more than 10 years.[119]

Plaintiffs also cite Peres (2016), a study of analgesic medication and the risk of epithelial ovarian cancer in African American women, for the proposition that

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[117] (Pls.' Opp'n at 55 (citing Trabert et al., *Aspirin, Nonaspirin Nonsteroidal Anti-Inflammatory Drug, and Acetaminophen Use and Risk of Invasive Epithelial Ovarian Cancer: A Pooled Analysis in the Ovarian Cancer Association Consortium*, 406(2) J. Nat'l Cancer Inst. 1 (2014) ("Trabert 2014 – Aspirin") (attached as Ex. A142 to Tersigni Cert.)).)

[118] Trabert 2014 – Aspirin at 5. Curiously, plaintiffs contend that defendants called the Trabert 2014 study "'flawed'" (Pls.' Opp'n at 55 (no citation in original)), when defendants said no such thing. Nor do defendants "reject[] the conclusions" of the authors, as plaintiffs contend. (*Id.*) Defendants merely pointed out that the results of the study were internally inconsistent because they only identified a decreased risk associated with aspirin use, not other NSAID drugs.

[119] Trabert et al., *Analgesic Use and Ovarian Cancer Risk: An Analysis in the Ovarian Cancer Consortium*, 111(2) J. Nat'l Cancer Inst. 137, 139-42 (2019) (attached as Ex. A141 to Tersigni Cert.).

NSAID use is inversely associated with EOC risk,[120] but – as set forth above – none of plaintiffs' experts relies on or discusses that study. Accordingly, the Peres (2016) study cannot possibly provide reliable support for plaintiffs' experts' opinions. And in any event, the Peres study looked at a very discrete question: whether NSAIDs had a protective effect among African American women.[121] In short, NSAID studies also cannot reliably support plaintiffs' experts' theories regarding inflammation.

Third, although plaintiffs acknowledge that the data on which their experts rely confirms that the association between PID and ovarian cancer "may be specific to a histologic subtype" (i.e., borderline tumors and, potentially, low-grade serous carcinomas) they maintain that it may also increase risk of high grade serous carcinoma.[122] In support of this position, plaintiffs point to one study by Stewart (2018), which is not discussed in any of plaintiffs' experts' reports.[123] In any event, a single cohort study showing a slight association between PID and high grade serous carcinoma does not make it biologically plausible that inflammation plays a role in the development of ovarian cancer. *See, e.g., Magistrini v. One*

120 (Pls.' Opp'n at 57-58 & nn.174-77 (citing Peres 2016).)

121 Peres 2016 (explaining that the study only examined data from studies involving African American women).

122 (Pls.' Opp'n at 57-58.) Notably, plaintiffs do not even respond to defendants' argument that endometriosis is not associated with high grade serous ovarian carcinoma. (*See* Defs.' Br. at 63-65.)

123 Stewart 2018.

Hour Martinizing Dry Cleaning, 180 F. Supp. 2d 584, 591 (D.N.J. 2002) ("[A]n association is not equivalent to causation. An association identified in an epidemiological study may or may not be causal. Assessing whether an association is causal requires an understanding of the strengths and weaknesses of the study's design and implementation, as well as a judgment about how the study findings fit with other scientific knowledge.") (citation omitted), *aff'd*, 68 F. App'x 356 (3d Cir. 2003). If anything, it merely highlights the point made in defendants' opening brief: the studies are inconclusive and require further investigation.[124]

For all of these reasons, plaintiffs (and their experts) are unable to point to any reliable scientific evidence that there is a biologically plausible connection between inflammation and ovarian cancer.

B. Plaintiffs' Experts' Theory That Perineal Talc Use Increases The Risk of Ovarian Cancer By Inhibiting MUC1 Antibodies Is Not Biologically Plausible.

As discussed in defendants' opening brief, Drs. Zelikoff and Saed's alternative theory that talcum powder use suppresses the level of anti-MUC1 antibodies – thereby rendering talcum powder users more susceptible to

[124] In any event, Stewart (2018) does little to help plaintiffs' case. That study found that, of the 33,335 women diagnosed with PID, only ***39*** were later diagnosed with high grade serous ovarian carcinoma. Stewart 2018 at 112. Notably, the study did ***not*** find a statistically significant reduction in risk for high grade serous ovarian carcinoma in women who had tubal ligation. *Id.* at 114.

developing ovarian cancer – is pure speculation.[125] This is because the studies cited by plaintiffs' experts are irrelevant, and there is no evidence of any relationship between MUC1 antibodies and the development of cancer.[126] In their opposition, plaintiffs attempt to resuscitate the studies cited by their experts. First, plaintiffs point to Cramer (2005) to support their claim that "anti-MUC1 antibodies reduce the risk of ovarian cancer."[127] The Cramer study assessed circulating levels of anti-MUC1 antibodies in 705 women without ovarian cancer and noted a slight statistical association between "nonuse of talc in genital hygiene" and increased circulating levels of anti-MUC1 antibodies.[128] But the Cramer study does not provide a reliable basis to draw any conclusions about talc use and anti-MUC1 antibodies; indeed, the American Association for Cancer Research published a Letter to the Editor stating that Cramer and his co-authors' conclusion in the article "about genital talc exposure increasing ovarian cancer risk via diminished antibody levels is not supported by their own data."[129] *See Muzzey v. Kerr-McGee Chem.*

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125 (Defs.' Br. at 66-69.)

126 (*See id.*)

127 (Pls.' Opp'n at 61 (citing Cramer et al., *Conditions Associated With Antibodies Against the Tumor-Associated Antigen MUC1 and Their Relationship to Risk for Ovarian Cancer*, 14(5) Cancer Epidemiol. Biomarkers Prev. 1125-31 (2005) ("Cramer 2005") (attached as Ex. 111 to Pls.' Opp'n)).)

128 Cramer 2005 at 1125 (abstract).

129 Muscat & Huncharek, *Talc and Anti-MUC1 Antibodies*, 14(11) Cancer Epidemiol. Biomarkers Prev. 2679 (2005).

Corp., 921 F. Supp. 511, 519 (N.D. Ill. 1996) (finding expert's causation opinion was unreliable where he relied on a study to support his causation opinion, but a later review of that study found the conclusions of the study unreliable); *see also Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146-47 (1997) (holding that "it was within the [d]istrict [c]ourt's discretion to conclude that the studies upon which the experts relied were not sufficient, whether individually or in combination, to support their conclusions that Joiner's exposure to PCB's contributed to his cancer").

Plaintiffs next turn to Karageorgi, a study examining whether there is any association between talc and endometrial cancer.[130] According to plaintiffs, Dr. Zelikoff's reliance on Karageorgi is appropriate because the results of that study are "not unique to endometrial cancer."[131] But the only reference in Karageorgi to MUC1 rests on the same 2005 Cramer study discredited in the American Association for Cancer Research journal. In any event, plaintiffs' argument misses the point. According to plaintiffs, the Karageorgi study is significant because it purportedly shows that "[u]sers of talcum powder have lower plasma levels of anti-

130 (*See* Pls.' Opp'n at 62 (citing Karageorgi et al., *Perineal Use of Talcum Powder and Endometrial Cancer Risk*, 19(5) Cancer Epidemiol. Biomarkers Prev. 1269 (2010) ("Karageorgi 2010") (attached as Ex. A84 to Tersigni Cert.)).)

131 (*Id.*)

MUC1 antibodies than non-users."[132] But even if the study did show some connection between talc use and anti-MUC1 antibodies – which, given its sole reliance on Cramer, is a dubious proposition – it still would not supply a "reliable" basis for Drs. Zelikoff and Saed's MUC1 theory because it does nothing to establish a relationship between anti-MUC1 antibodies and the ***development of cancer***. Indeed, as defendants noted in their opening brief, not a single one of plaintiffs' 21 putative experts draws this connection.[133] Plaintiffs offer no response to this argument, or to defendants' experts, who affirmatively state that there is "no evidence" of any association between anti-MUC1 antibodies and cancers of any type.[134]

In short, plaintiffs' experts' MUC1 hypothesis not only has no basis in the relevant scientific literature, but is also irrelevant to plaintiffs' efforts to establish a mechanism by which talc could cause ovarian cancer. Accordingly, these opinions, too, should be excluded. *See, e.g.*, *Henricksen*, 605 F. Supp. 2d at 1176 (rejecting expert causation opinions for lack of biological plausibility where the relevant studies "make clear that the connection" between the substance and disease at issue "is at this point in time only a hypothesis in need of further investigation").

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132 (*Id.* (quoting Karageorgi 2010).)

133 (Defs.' Br. at 67-68.)

134 (*Id.* at 68 (citing Neel Rep. at 23; Moore Rep. at 37).)

V. DR. ZELIKOFF'S RAMPANT PLAGIARISM OF SIGNIFICANT ASPECTS OF HER REPORT RENDERS HER OPINIONS INHERENTLY UNRELIABLE.

Finally, Dr. Zelikoff's opinions are unreliable because she conceded that significant portions of her report are copied directly from sources that she fails to credit. In their opposition, plaintiffs do not deny that Dr. Zelikoff plagiarized portions of her report. Instead, they attempt to defend Dr. Zelikoff's plagiarism on the ground that the copied portions of her report consist only of "background information and points of common knowledge" and therefore do not affect the reliability of her opinion.[135]

Plaintiffs are wrong. Far from merely copying "background" information, Dr. Zelikoff plagiarized material that goes to the heart of her opinion. Moreover, unlike the cases cited in plaintiffs' brief – where, for example, an expert "fail[ed] to include quotation marks to indicate that portions of his opinion . . . were direct quotations of the sources he cited in a footnote to those paragraphs," *In re Processed Egg Prods. Antitrust Litig.*, No. 08-md-2002, 2016 WL 4547207, at *5 (E.D. Pa. Aug. 31, 2016) (cited in Pls.' Opp'n at 63 n.198) – Dr. Zelikoff wholly failed to attribute the sources that she copied anywhere in her report. For example:

- Dr. Zelikoff states that "[l]ymph capillaries remove the large protein molecules and other particulate matter from the tissue spaces of the lung. Thus, cellular debris and foreign particles . . . are conveyed to the regional

[135] (Pls.' Opp'n at 64.)

lymph nodes."[136] This statement is central to her theory that talcum powder can reach a woman's ovaries through inhalation.[137] Moreover, the statement appears to be directly copied from a website – www. mananatomy.com – that Dr. Zelikoff does not cite anywhere in her report.[138]

- More than half of Dr. Zelikoff's section on genetic mutations was copied from a report titled "Mutations and Health" published by Genetics Home Reference.[139] These copied paragraphs undergird Dr. Zelikoff's opinion that talc can cause gene mutations that increase the risk of cancer. Dr. Zelikoff acknowledged that "there are sentences that are identical" in her report and in the "Mutations and Health" report and agreed that, "if [she] had to do [her report] over, [she] would have put quotation marks around" the passages at issue.[140] Despite this concession, Dr. Zelikoff has not submitted an amended report correcting this and other instances of plagiarism. *See In re Processed Egg Prods.*, 2016 WL 4547207, at *5 (noting that, after being questioned at his deposition about his failure to cite sources for particular statements in his report, the expert "issued an errata report correcting the[] errors").

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136 (Zelikoff Rep. at 15.)

137 (*Id.* at 14-15 (purporting to provide a "scientific premise" for the notion that "particles of a certain size" – like talc – can move "throughout the body").)

138 *See Functions of Lymphatic System*, MANanatomy.com, http://www.mananatomy.com/basic-anatomy/functions-lymphatic-system (last visited June 12, 2019) (attached as Ex. J7 to 2d Suppl. Tersigni Cert.).

139 (Zelikoff Dep. Ex. 15 (attached as Ex. B52 to 2d Suppl. Tersigni Cert.) (highlighting paragraphs in Dr. Zelikoff's expert report that were taken from Genetics Home Reference).)

140 (Zelikoff Dep. 100:7-16, 97:22-24.) Dr. Zelikoff also admitted that other portions of her report were copied verbatim from other sources. (*See, e.g.*, *id.* 102:21-106:8 (acknowledging that several sentences from a Simone Reuter article were copied without quotation or acknowledgment); *id.* 107:14-109:22 (acknowledging that five portions of EnvironmentalChemistry.com are copied verbatim in her report); *id.* 115:17-119:17 (defending copying of four sentences of Rakoff-Nahoum publication by claiming, incorrectly, that author she copied also did not give references); *id.* 119:22-121:13 (acknowledging having copied language from OSHA publication without citation).)

These and other examples set forth in defendants' opening brief and in Dr. Moore's report make clear that Dr. Zelikoff's plagiarized opinions are not merely "background information and points of common knowledge pulled from various sources,"[141] but rather reflect substantive conclusions that were pulled from identifiable (and arguably unscientific) sources that she decided not to reference. For this reason, too, Dr. Zelikoff's opinions are unreliable and should be excluded.

CONCLUSION

For the foregoing reasons, and those set forth in the J&J defendants' opening memorandum, the Court should exclude plaintiffs' experts' biological plausibility opinions.

[141] (Pls.' Opp'n at 64.)

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Respectfully submitted,

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